

**IN THE UNITED STATES DISTRICT COURT
FOR THE SOUTHERN DISTRICT OF WEST VIRGINIA
AT CHARLESTON**

IN RE ETHICON, INC., PELVIC REPAIR SYSTEM PRODUCTS LIABILITY LITIGATION	Master File No. 2:12-MD-02327 MDL 2327
THIS DOCUMENT RELATES TO: WAVE 4 CASES LISTED IN MOTION EXHIBIT A	JOSEPH R. GOODWIN U.S. DISTRICT JUDGE

**DEFENDANTS' REPLY IN SUPPORT OF MOTION TO EXCLUDE
THE OPINIONS AND TESTIMONY OF VLADIMIR IAKOVLEV, M.D.**

Defendants Ethicon, Inc., Ethicon LLC, and Johnson & Johnson (collectively, “Ethicon”) submit this Reply in Support of their Motion to Exclude the Testimony and Opinions of Vladimir Iakovlev, M.D. [Doc. 3619].

I. Dr. Iakovlev’s Opinions Regarding Complications Allegedly Caused By Ethicon Mesh Products Are Unreliable.

A. Dr. Iakovlev’s opinions regarding complications do not relate to the field of pathology.

Plaintiffs argue that Dr. Iakovlev should be able to offer opinions regarding complications based on his review of pathology slides because he does so in the course of his practice as a pathologist. Plaintiffs’ argument appears to be predicated on a deeply flawed understanding of what pathologists actually do and this Court’s Wave 1 *Daubert* Order. *See generally* Mem. Op. and Order (*Daubert* Motion re: Vladimir Iakovlev, M.D.) [Doc. 2710] (“Wave 1 *Daubert* Order”).

The Court's Wave 1 Order permits Dr. Iakovlev to offer opinions as to whether tissue he analyzed is normal or abnormal. Indeed, Ethicon does not dispute that a pathologist can opine that tissue exhibits inflammation or scarring, for example.

What Dr. Iakovlev *cannot* do is to use a finding of abnormal tissue as a basis for opining that a plaintiff suffered a clinical complication due to that abnormality. *See* Wave 1 *Daubert* Order, at 8-9. This is not pathology; by taking this additional step, Dr. Iakovlev is offering a clinical urogynecological opinion.

Nothing in Dr. Iakovlev's education, training, or experience as a pathologist permits him to draw such a causal conclusion. Because opinions regarding the complications allegedly caused by Ethicon mesh products exceed the scope of Dr. Iakovlev's qualifications as a pathologist, the Court should preclude him from offering any such opinions at trial. *See* Fed. R. Evid. 702.

B. Dr. Iakovlev's failure to use a control renders his opinions regarding complications unreliable.

In its Wave 1 *Daubert* Order, the Court excluded Dr. Iakovlev's "complications opinions based on his examination of explanted mesh samples without the use of a control sample," on the grounds that such opinions were not the product of "a sufficiently reliable methodology." Wave 1 *Daubert* Order, at 8-9. In a re-do of their Wave 3 briefing, Plaintiffs argue that the Court's ruling was erroneous because not only is there "no need for a control sample at all, for a pathologist's opinions to be reliable[.]" but "the use of a control sample is not appropriate for a diagnostic pathology work." Resp. at 6. Plaintiffs claim that pathologists "use their knowledge of normal anatomy and histology (not controls) to detect the changes (abnormalities) and classify them as either the cause (etiology) or the result (disease)." *Id.*

Plaintiffs' argument is unsupported by medical literature and inconsistent with basic principles of science. Plaintiffs rely only on a self-serving declaration submitted by Dr. Iakovlev,

which is merely a longer version of the affidavit Dr. Iakovlev submitted with Plaintiffs' Wave 3 response.¹ Yet again, Dr. Iakovlev fails to identify any literature for the proposition that a pathologist does not need to use a control in offering causal opinions. *See generally* Resp. Ex. T, Iakovlev Dec. Indeed, Dr. Iakovlev's declaration amounts to nothing but *ipse dixit*.

1. The Court properly excluded Dr. Iakovlev's opinions regarding complications.

In its Wave 1 *Daubert* Order, this Court precluded Dr. Iakovlev from offering opinions regarding complications based on his review of pathology slides because he failed to use a proper control. Wave 1 *Daubert* Order, at 8-9. The Court reasoned that, in the absence of a proper control, Dr. Iakovlev cannot rule out the fact that the patients suffering from a particular complication may have the same pathological presentation as patients who do not.

The Court's ruling on this point is consistent with the standard practice of pathology and fundamental principles of science. Plaintiffs did not identify any authority suggesting that pathology is somehow exempt from such core scientific principles. *Cf.* Reply Ex. GG, Robbins & Cotran Pathologic Basis of Disease, at 11 (8th ed. 2010) (explaining that pathology "serves as the bridge between the basic sciences and clinical medicine, and is the scientific foundation for all medicine.").

Indeed, although the crux of Plaintiffs' argument is pathologists do not use controls in their practice, they fail to cite any scientific or medical literature supporting their assertion. *See* Resp. at 5-7. Instead, Plaintiffs base their argument solely on a declaration by Dr. Iakovlev and his expert report. *See id.* But neither Dr. Iakovlev's declaration nor his expert report identify any literature supporting the notion that controls are unnecessary in the field of medicine or the

¹ Compare Resp. Ex. T, Declaration of Vladimir V. Iakovlev, MD, FRCPC, FCAP with Ex. I, Affidavit of Vladimir Iakovlev, MD, FRCPC, FCAP (Oct. 10, 2016) (attached to Plaintiffs' Wave 3 response as Ex. I).

subspecialty of pathology. *See generally* Resp. Ex. T, Iakovlev Dec.; Mot. Ex. D, Expert Report of Vladimir Iakovlev.

Although Dr. Iakovlev's declaration discusses a handful of pathology texts, none of these sources actually stands for the proposition that controls are unnecessary in the field of pathology. *See* Resp. Ex. T, Iakovlev Dec. at ¶¶ 7-11. Indeed, Dr. Iakovlev's use of scientific literature in his declaration is limited to highly general principles of pathology and the pathologist's relationship to clinical medicine. *See id.*

Tellingly, Dr. Iakovlev does not cite any scientific or medical authority whatsoever in his discussion of the use of controls. *See id.* at ¶¶ 12-21.² Rather, Dr. Iakovlev describes what he believes to be the appropriate use of controls, and declares that he does not need them. This is textbook *ipse dixit*, which is not rendered any more scientifically reliable by its incorporation in a declaration. *See Gen. Elec. Co. v. Joiner*, 522 U.S. 136, 146 (1997) ("nothing in either *Daubert* or the Federal Rules of Evidence requires a district court to admit opinion evidence that is connected to existing data only by the *ipse dixit* of the expert.").

2. Plaintiffs' assertion that it is impossible or inappropriate for pathologists to use a control is simply incorrect.

In their response, Plaintiffs argue that it is "impossible" and "not appropriate" for a pathologist to use a control. Resp. at 6-7. Indeed, Plaintiffs claim that a pathologist cannot use a control in the context of this litigation because "it would make no sense to explant [] mesh from a woman experiencing no complications." Plaintiffs' arguments are without merit.

As an initial matter, it is common for mesh to be explanted for reasons other than erosions, pain, or dyspareunia. Plaintiffs' unsupported assertion to the contrary makes no sense.

² Dr. Iakovlev claims in his declaration that sources like Robbins & Cotran are the basis of his methodology, but his expert report shows that his sole reference to that text is for the proposition that "[i]n adult mammals, regeneration of soft tissue may occur to a limited degree in some animals." Mot. Ex. D, Iakovlev Report at 6, 127. Any suggestion that these texts constitute the foundational predicate of Dr. Iakovlev's methods is disingenuous, at best.

In addition, Plaintiffs' position is belied by the fact that other scientists have compared asymptomatic and symptomatic explants. For example, in a study by Hill, the authors used the scientific method to identify whether the morphological presentation of inflammation causes the clinical symptom of pain. *See* Mot. Ex. C, A. Hill, *Histopathology of Excised Midurethral Sling Mesh*, 26 Int'l Urogynecology J. 591 (2015). To do so, the Hill study authors compared the histopathology findings regarding explants from patients complaining of pain with those who did not. *Id.* Contrary to their own hypothesis, the authors found that pain was not associated with increased inflammation and scarring. *Id.* at 592-93.

Thus, the Hill study not only demonstrates the scientific significance of using a control, but it directly refutes Dr. Iakovlev's unsupported opinion that scarring and inflammation cause pain. Notably, Dr. Iakovlev has never made such a systematic comparison of asymptomatic and symptomatic tissues to provide a scientifically sound basis for his opinions. For this reason, his opinions are nothing but speculation.

Plaintiffs cannot avoid bedrock scientific principles by declaring controls unnecessary simply because Dr. Iakovlev states that he does not need one. Plaintiffs' arguments are contrary to the scientific method, and should be rejected by this Court.

3. Plaintiffs misstate the law under *Daubert*.

Finally, Plaintiffs claim that Dr. Iakovlev should be permitted to opine about the complications without incorporating a control in his analysis because he does not use a control in his normal practice. *Resp.* at 6-7. In attempting to support their argument, Plaintiffs assert that the "fundamental focus of the *Daubert* inquiry is whether the expert has employed the same 'intellectual rigor' in his work for the case *as he would* in normal practice." *Id.* at 7 (emphasis added). Plaintiffs misunderstand *Daubert* and its progeny.

The case law clearly states that the proper metric is the “practice of *an* expert in the relevant field,” not the practice of the expert himself. *See Kumho Tire Co. v. Carmichael*, 526 U.S. 137, 152 (1999); *Cooper v. Smith & Nephew, Inc.* 259 F.3d 194, 200 (4th Cir. 2001); *Eghnayem v. Boston Sci. Corp.*, 57 F. Supp. 3d 658, 675 (S.D. W. Va. 2014). But pathologists do not typically do what Dr. Iakovlev does in this litigation. Additionally, under Plaintiffs’ nonsensical interpretation, an expert’s opinion would be reliable—even if he failed to comply with the scientific method—so long as he used the same baseless methodology in his practice. Nothing in *Daubert* or its progeny supports such an absurd result.

Plaintiffs cannot transform Dr. Iakovlev into the arbiter of the reliability of his own opinions, and the Court should reject Plaintiffs’ arguments on this basis.

II. Dr. Iakovlev’s Failure To Test His Hypothesis That Degraded Prolene Traps Histological Stains Shows That His Degradation Opinions Are Unreliable.

A. Dr. Iakovlev’s “bark” theory is the only aspect of his degradation opinions bearing any relationship to his qualifications as a pathologist.

In its Motion, Ethicon acknowledged that, in its Wave 1 *Daubert* Order, the Court disagreed with Ethicon’s position that Dr. Iakovlev’s bark theory is central to all of his degradation opinions. Mem. at 4-5. To clarify its argument, Ethicon explained that Dr. Iakovlev’s bark theory is the only part of his degradation opinions that actually relates to his qualifications as a pathologist. Ethicon further observed that without his bark theory, Dr. Iakovlev simply seeks to inform the jury that Prolene degrades based on his literature review. This constitutes a materials science opinion, not a pathology opinion.

Plaintiffs’ response actually reinforces Ethicon’s argument. Plaintiffs identify five steps that Dr. Iakovlev supposedly followed in developing his degradation opinions. Specifically, Plaintiffs state that Dr. Iakovlev (1) reviewed mesh explants; (2) prepared and reviewed that pathology using the methods he uses as a clinical pathologist; (3) provided photomicrographs of

the explants “as representative images of the degradation and changes that can occur *in vivo*”; (4) supported his opinions based on his literature review; and (5) gave Ethicon an opportunity to review his slides. Resp. at 8-9.

Steps 1-3 of Plaintiffs list simply refer to Dr. Iakovlev’s bark theory analysis, *i.e.*, he reviewed explants and detected evidence of degradation using histological stains and light microscopy. Stripped of this unreliable analysis, it is clear that Dr. Iakovlev would seek to inform the jury that Prolene degrades based solely on his review of literature. This is a polymer science opinion that is beyond Dr. Iakovlev’s qualifications as a pathologist.

Because Plaintiffs make no other effort to rebut Ethicon’s position, their reliance on this Court’s Wave 1 Order is misplaced.

B. Plaintiffs’ efforts to distinguish *Nease* are meritless.

In its Motion, Ethicon argued that, under the Fourth Circuit’s decision in *Nease v. Ford Motor Co.*, 848 F.3d 219 (4th Cir. 2017), Dr. Iakovlev’s degradation opinions are unreliable due to a lack of testing to verify his hypothesis. Mem. at 3–6. Plaintiffs seek to distinguish *Nease* on a number of grounds, but none of their efforts overcome the basic flaw in Dr. Iakovlev’s methodology: he failed to validate his hypothesis through testing or scientific literature.

For instance, Plaintiffs try to dismiss the importance of *Nease* on the grounds that testing “has long been a factor considered by courts when considering the reliability of an expert’s opinion[,]” but it is not a “requirement.” Resp. at 4. However, *Nease* recognized that testing is an “especially important factor for guiding a court in its reliability determination.” 848 F.3d at 231.

Here, as in *Nease*, Dr. Iakovlev’s failure to test his hypothesis deprives his bark theory of reliability. Dr. Iakovlev could have conducted testing to confirm his degradation opinions, but he failed to do so. *See* Mem. at 3-6. As it stands, his opinion that histological stain is trapped in the

degraded surface of Prolene fibers is simply an untested hypothesis and “it thus is not knowledge.” *Nease*, 848 F.3d at 231 (citation omitted).

Notably, Plaintiffs’ assertion that Dr. Iakovlev “and other scientists have *seen* the bark on explanted mesh and confirmed its properties through a panoply of well-accepted processes” is misleading. Resp. at 4. Although Dr. Iakovlev and other experts for Plaintiffs may claim to observe bark on mesh fibers, they have failed to “confirm its properties” through any reliable scientific methodology. Indeed, none of Plaintiffs’ experts have conducted any testing to demonstrate that this bark is composed of degraded Prolene. Tellingly, Plaintiffs failed to identify a single one of this alleged “panoply of well-accepted processes.”

In addition, despite Plaintiffs’ suggestion to the contrary, Ethicon never argued that testing is an absolute precondition to the admissibility of expert opinion. Rather, Ethicon explained that Dr. Iakovlev failed to test the hypothesis underlying his degradation opinions, and there is no support for his methodology in the scientific literature. *See* Mem. at 3-10. Thus, Dr. Iakovlev’s degradation opinions—like the opinions at issue in *Nease*—cannot satisfy *Daubert*’s reliability requirement. *See Nease*, 848 F.3d at 232 (finding that expert’s opinion could not survive reliability prong because it was untested, had not been subjected to peer-review, and there was no way to assess its potential error rate).

C. Dr. MacLean’s control experiment is relevant and reliable.

As explained in Ethicon’s Motion, Dr. Steven MacLean conducted the test that Dr. Iakovlev has refused to perform: a simple control experiment to assess the validity of Dr. Iakovlev’s hypothesis that degraded Prolene traps histological stain such that it can be observed as “bark” using light microscopy. *See* Mem. at 6–8. Based on a reliable and repeatable methodology, Dr. MacLean’s control experiment showed that none of the Prolene fibers trapped stain, which invalidates Dr. Iakovlev’s methodology. *Id.*

1. Dr. MacLean's control experiment shows that Dr. Iakovlev failed to follow a reliable scientific methodology.

Plaintiffs argue that Dr. Iakovlev did not need to conduct “confirmatory laboratory testing.” Resp. at 10. Plaintiffs misunderstand the point of a control experiment, as well as the scientific method. A control experiment is not “confirmatory”; rather, it is the manner in which a test is validated. Without a control experiment, Dr. Iakovlev has no basis for assuming that his methodology actually does what he claims. Thus, his opinions are little more than a guess.

Similarly, Plaintiffs argue that Dr. MacLean's control experiment does not constitute a basis for excluding Dr. Iakovlev's opinions because it reflects “conflicting opinions of experts[.]” See Resp. at 11. This is false.

Dr. MacLean's control experiment does not merely permit him to reach a different conclusion than Dr. Iakovlev, as Plaintiffs claim. Rather, the significance of Dr. MacLean's work is that it represents the control experiment that Dr. Iakovlev should have conducted *before* offering his conclusions. Put differently, even without Dr. MacLean's results, Dr. Iakovlev's opinions should be excluded as unreliable because he failed to test his hypothesis. The fact that Dr. MacLean's control experiment actually disproves Dr. Iakovlev's hypothesis further demonstrates the unreliability of Dr. Iakovlev's opinion.

Furthermore, although Plaintiffs now seek to downplay Dr. Iakovlev's admission that he was testing his hypothesis, (Resp. at 10-11), Dr. Iakovlev's testimony on this point is clear and shows that he offered conclusions based on a theory he has not tested, (Mem. at 5-8).

2. Dr. MacLean's *in vitro* control experiment is relevant.

Plaintiffs argue that Dr. MacLean's *in vitro* control experiment is irrelevant to Dr. Iakovlev's *in vivo* opinions because Dr. Robyn Prueitt—a toxicologist Ethicon did not disclose

as an expert in this litigation—testified that *in vitro* testing does not replicate *in vivo* conditions. *See* Resp. at 11–12.

As an initial matter, it is clear from the very same page of Dr. Prueitt’s deposition cited by Plaintiffs that her testimony specifically pertained to a well-known toxicological concept. *See* Resp. Ex. D, Prueitt 10/22/15 Dep. Tr. 89:1–90:4. Specifically, Dr. Prueitt explained that *in vitro* testing is primarily useful as a screening mechanism, because if highly concentrated doses of the substance at issue applied directly to cells do not cause toxicological effects, no such effects would be expected *in vivo*. *See id.* As Dr. Prueitt’s testimony clearly dealt with questions of toxicology, Plaintiffs’ argument is without merit.³

Moreover, Dr. MacLean used chemical and QUV-oxidation methods that far exceed the oxidative capacity of anything in the pelvic floor. *See* Mot. Ex. J, MacLean Report at 78-79. The fact that the Prolene fibers did not trap stain indicates that Prolene fibers would not do so after exposure to *in vivo* conditions. Plaintiffs’ attempt to undermine Dr. MacLean’s testing using basic principles of cytotoxicology is not only inapposite, but it contradicts their argument.

3. Plaintiffs ignore the fact that Dr. MacLean’s control experiment analyzed Prolene fibers subjected to two separate oxidation methods, and confirmed cracking in QUV-treated Prolene fibers.

Plaintiffs suggest that Dr. MacLean’s control experiment is unreliable because it allegedly did not actually analyze oxidized Prolene. *See* Resp. at 12. Plaintiffs claim that Dr. MacLean erred by following a protocol used by Plaintiffs’ own experts—Drs. Guelcher and Dunn—which called for exposing mesh samples to a chemical oxidative medium for five weeks.

³ Plaintiffs misunderstand the term *in vitro*, which refers to the study of cells and other biological materials outside their normal environment. *See, e.g., Bourne ex rel. Bourne v. E.I. DuPont de Nemours & Co., Inc.*, 189 F. Supp. 2d 482, 489 n.14 (S.D. W. Va. 2002) (“*In vitro* tests involve the exposure of isolated cell systems to a particular substance under controlled laboratory conditions within a test tube or petri dish.”). Dr. MacLean conducted an *ex vivo* control experiment that focused on the question of whether intentionally oxidized Prolene fibers can trap histological stains. *See* Mot. Ex. J, Expert Report of Dr. Steven MacLean (“MacLean Report”) at 76-96. The inquiry was focused on the effect of stains to the fiber itself, not the effect of the fiber on tissues or cells.

See id. Plaintiffs assert that Dr. MacLean should have followed Dr. Iakovlev’s approach, which involves exposing the mesh to the chemical oxidative medium for at least 18 months. *Id.*

Plaintiffs appear to be oblivious to the fact that this argument is directly at odds with their assertion that Dr. Iakovlev’s incomplete testing is for a different purpose. *See Resp.* at 10. Moreover, Plaintiffs fail to acknowledge Dr. Iakovlev’s ongoing refusal to follow his own approach—he still has not tested his theory even though it has now been far more than 18 months. Mot. Ex. B, Iakovlev 3/21/16 (*Stubblefield*) Dep. Tr. 64–65. Plaintiffs’ argument—that Dr. MacLean’s testing is irrelevant because he “did not even do the test that Dr. Iakovlev” has not done—is ridiculous. *See Resp.* at 12.

Plaintiffs also ignore the fact that Dr. MacLean subjected Prolene samples to two oxidation methods. *See* Mot. Ex. J, MacLean Report at 76-79.⁴ In addition to following the protocol used by Drs. Guelcher and Dunn that Plaintiffs now dismiss as invalid, Dr. MacLean ensured that at least some Prolene fibers would oxidize by subjecting one batch of Prolene samples to QUV. *Id.* QUV treatment is widely recognized in scientific literature to oxidize polypropylene, including Prolene. *Id.*; *see also* Reply Ex. HH, Benight 10/13/15 Dep. Tr. 214:6–13 (QUV treatment is “covered in over hundreds of literature articles -- including intentionally oxidizing polymer samples”).

Dr. MacLean conducted SEM on the samples, and found that while the QUV-treated fibers exhibited clear evidence of surface cracking, the chemically oxidized samples did not. *See* Mot. Ex. J, MacLean Report at 80-82. With respect to the QUV-treated fibers subjected to Dr.

⁴ As explained in greater detail in Ethicon’s responses Plaintiffs’ motions to exclude Dr. MacLean’s opinions, Plaintiffs’ arguments regarding his opinions and control experiment are without merit. *See* Notice of Adoption of Prior Daubert Response Regarding Steven MacLean for Wave 4 [Doc. 3768] (adopting response in Wave 2 [Doc. 2552]).

Iakovlev's staining protocol, Dr. MacLean confirmed surface cracking using SEM. *See, e.g., id.* at 80 (fig. 17), 81 (fig. 18), 82 (fig. 19).

Notably, Plaintiffs do not even mention the QUV-treated samples used in the control experiment. *See* Resp. at 11–12. Plaintiffs' arguments that Dr. MacLean's control experiment was unreliable are meritless, and should be rejected by this Court.

D. Dr. Iakovlev's testimony undercuts Plaintiffs' efforts to downplay his testing.

Although Plaintiffs argue that Dr. Iakovlev's testing does not address whether the allegedly degraded outer layer of a mesh fiber traps histological stain (Resp. at 10–11), Dr. Iakovlev's testimony belies their claim. Indeed, on the very same page of Dr. Iakovlev's deposition transcript to which Plaintiffs cite, Dr. Iakovlev acknowledges that this is the precise purpose of his testing:

Q. And as a part of your experiment do you then intend to see whether—if you are able to oxidize polypropylene, according to your visual observation by light microscopy, will you then see whether the oxidized polypropylene holds stain?

A. Yes, that's the way to see it. This just becomes porous and after absorbs stain.

See Mot. Ex. G, Iakovlev 9/11/15 Dep. at 45:9–16 (emphasis added); *see also id.* at 44:12–26 (agreeing that the “reason why you're doing this test is to determine whether, first, after 18 months this polypropylene will oxidize due to exposure to this chemical mixture” using light microscopy).

Even assuming Plaintiffs are correct and Dr. Iakovlev is not performing these tests to verify his hypothesis, his failure to recognize the necessity of conducting a control experiment to validate his theory only confirms that he does not understand the scientific method.

E. No scientific or medical literature supports Dr. Iakovlev's “bark” theory.

Plaintiffs claim that Ethicon's argument that “there is no scientific or medical evidence to support Dr. Iakovlev's opinions concerning degradation ‘bark’ from explanted mesh *in vivo* is

simply wrong.” Resp. at 12. Remarkably, in the very next paragraph, Plaintiffs apparently concede that no such literature actually supports Dr. Iakovlev’s bark theory by asserting that the lack of such support is immaterial so long as Dr. Iakovlev used a “reliable methodology when studying the explanted mesh samples[.]” *Id.* at 13.

Although Plaintiffs attempt to support Dr. Iakovlev’s bark theory by pointing to certain articles and internal Ethicon documents, a closer review of these papers reveals that they fail to support Plaintiffs arguments. *See* Resp. at 12-16. Indeed, only one of the papers employed methods similar to those used by Dr. Iakovlev, and that internal Ethicon document is subject to the same criticisms as Dr. Iakovlev’s methodology.

Specifically, the researchers in the 1984 “Ethicon Research Foundation” test conducted their analysis without running a control experiment to validate the underlying hypothesis that degraded Prolene would hold stain. *See* Reply Ex. II, ETH.MESH.15955462. Dr. MacLean has performed that experiment, and invalidated this hypothesis. *See* Mem. at 6–7. Plaintiffs ask this Court to hold Ethicon’s state of scientific knowledge to testing that took place over 30 years ago without regard for advances in scientific methods and understanding, including the fact that the hypothesis underlying the testing has now been disproven. The Court should reject Plaintiffs’ invitation to ignore the scientific method, which necessarily requires “subjecting testable hypotheses to the crucible of experiment in an effort to disprove them.” *U.S. v. Bynum*, 3 F.3d 769, 773 (4th Cir. 1993).

Plaintiffs’ argument that the Court’s focus should be on Dr. Iakovlev’s methods is correct. The problem is that Plaintiffs disregard the fact that the absence of scientific literature supporting Dr. Iakovlev’s opinions, coupled with his failure to test his hypothesis, speaks *directly* to his poor methodology. *See* Mem. at 8-9.

Ethicon's argument is not, as Plaintiffs claim, merely that Dr. Iakovlev's conclusions have not been published or are simply incorrect. *See* Resp. at 12-13. Rather, as discussed in Ethicon's Motion, Dr. Iakovlev's opinions are not based on a reliable scientific methodology because he has not tested the basis for his degradation opinions, and no scientific or medical literature supports Dr. Iakovlev's opinions regarding degradation bark. *See* Mem. at 4-9 (explaining Dr. Iakovlev's own papers are the only publications that support his theories, and even his own papers call his theories into question).

F. Dr. Iakovlev's degradation theory is neither based in nor supported by scientific literature.

In its Motion, Ethicon argued that Dr. Iakovlev's bark theory is—by his own admission—not based in previous scientific literature. Mem. at 8-9. Given that Dr. Iakovlev failed to validate his hypothesis through testing, his failure to ground his theory on scientific literature demonstrates that his methods are unreliable. *See id.*

Plaintiffs do not actually respond to Ethicon's arguments, which specifically addressed Dr. Iakovlev's bark theory. Resp. at 8-11.⁵ Rather, Plaintiffs shift the focus of the inquiry by asserting that Dr. Iakovlev's opinions "that Ethicon's mesh products degrade *in vivo* are based on the well-documented medical and scientific literature that he cites in his report, as well as the Ethicon documents that confirm the existence of degradation." *Id.* at 9. Indeed, Plaintiffs claim that Dr. Iakovlev's degradation opinions are supported by "dozens of published scientific articles and numerous Ethicon documents in his 30-page reliance list," and that he "details his degradation opinions, supporting each such opinion with a wealth of published literature as well as internal Ethicon degradation testing and sworn testimony." *Id.* at 8.

⁵ To be clear, Ethicon does not concede that the articles on which Dr. Iakovlev relies actually support his opinions. Rather, as discussed above and in the Motion, Ethicon submits that the lack of reliability of Dr. Iakovlev's bark theory renders all of his degradation opinions beyond his qualifications as a pathologist.

Even assuming *arguendo* that the materials to which Plaintiffs refer do support Dr. Iakovlev's other degradation opinions, the fact of the matter is that Plaintiffs are playing a shell game. Neither Dr. Iakovlev nor Plaintiffs identified any peer-reviewed literature that validates Dr. Iakovlev's theory that degraded Prolene traps histological dye such that it can be detected using a microscope. For this reason, Dr. Iakovlev's bark theory is methodologically unsound.

Additionally, Plaintiffs' suggestion that each of the 600 articles and Ethicon documents in Dr. Iakovlev's reliance list support his degradation opinions is absurd. *See id.* at 18. And while Plaintiffs repeatedly claim that Dr. Iakovlev's opinions are based on scientific literature, they do not identify a single peer-reviewed study supporting his degradation opinions. *See id.* at 8–17.

Moreover, as Ethicon explained in its Motion, Dr. Iakovlev's own publications demonstrate that the opinions he seeks to offer to a reasonable degree of scientific certainty in Court are not supported by scientific literature other than his own writings, one of which even concedes that "the question of whether polypropylene degrades *in vivo* has not been fully resolved, despite decades of use." Mem. at 8-9; *see also* Mot. Ex. P, Blaivas, *Safety Considerations for Synthetic Sling Surgery*, Nature Rev. Urology, at 17 (2015).

Thus, Dr. Iakovlev's own writings belie Plaintiffs' suggestion that his opinions are consistent with the body of scientific literature. Accordingly, the Court should exclude Dr. Iakovlev's opinions regarding degradation in this case.

G. The scientific literature and Dr. Iakovlev's own writings do not support his opinion that degradation causes complications *in vivo*.

In its Motion, Ethicon explained that Dr. Iakovlev seeks to inform the jury that science shows that Prolene degradation causes complications in patients, despite the fact that he failed to base his opinion on testing or identify any support in the literature demonstrating that any such degradation actually does so. Mem. at 9-10. Ethicon also noted that Dr. Iakovlev's, which only

state that degradation “may” have a role in complications, are not a sufficient basis for him to opine in this litigation that degradation “does” cause complications in patients. *See id.* at 10. Although Ethicon is aware of this Court’s Wave 1 *Daubert* Order, Ethicon respectfully submits that *Nease* makes clear that expert opinion that is “unsupported by any evidence such as test data or relevant literature in the field” should be excluded as unreliable. *See Nease*, 848 F.3d at 234.

As Plaintiffs essentially adopted their Wave 1 response on this point, they did not directly respond to the arguments raised in Ethicon’s Wave 4 Motion. The arguments raised in Plaintiffs’ response fail to demonstrate that Dr. Iakovlev’s opinions rest on a reliable scientific footing.

Tellingly, Plaintiffs did not actually deny that the scientific literature does not show that degradation causes complications *in vivo*. *See Resp.* at 16-17. Instead, Plaintiffs claim that Dr. Iakovlev is qualified by training to opine on these issues, and point to a previous order issued by this Court that Ethicon respectfully submits is distinguishable from this case. *See id.* Specifically, Plaintiffs’ argument fails because the evidence on which Ethicon bases its arguments in this litigation was not before the Court when it issued its decision in *Edwards*.

In arguing that Dr. Iakovlev’s degradation opinions are based on the “weight of [the] evidence,” (*Resp.* at 17), Plaintiffs ignore the fact that the evidence contradicting his opinions includes his own publications (*Mem.* at 9–10). Grasping at straws, Plaintiffs assert that Ethicon’s arguments are based on “selective quotes” and “out of context citations” from Dr. Iakovlev’s writings. *Resp.* at 16-17. But Plaintiffs do not dispute that Dr. Iakovlev’s out-of-court writings concede that the scientific literature has not shown that degradation causes complications in patients. *See id.* It is unclear what further context is necessary to observe that there is an important scientific difference between asserting that “A *may* cause B” and “A *does* cause B.”

III. Dr. Iakovlev's Theory that All Erosions Are Associated with Infection Is Unsupported by Scientific Literature and Relies on Unsound Logic.

Dr. Iakovlev's opinion that Ethicon mesh products cause erosions in patients that necessarily prove that the patient suffered from an infection is unreliable. Mem. at 17-18. Specifically, Ethicon showed that Dr. Iakovlev made no effort to adhere to any diagnostic criteria in developing his opinions regarding infection or follow any reliable methodology. *See id.* In Wave 1, this Court excluded Dr. Iakovlev's infection opinion as unreliable on the grounds that it was "simply not supported with cited scientific literature." Wave 1 *Daubert* Order, at 11.

In their response, Plaintiffs simply ignore the Court's Wave 1 *Daubert* Order, and instead re-assert their arguments from their Wave 1 responsive briefing. *See* Resp. at 19. Plaintiffs failed to identify any basis for this Court to reconsider its Wave 1 *Daubert* Order. The Court should reject Plaintiffs' arguments on this basis alone.

Moreover, as discussed in Ethicon's Wave 1 reply, Plaintiffs' arguments are without merit. Indeed, in attempting to support Dr. Iakovlev's theory that all erosions are associated with infection, Plaintiffs do not cite to any peer-reviewed medical literature. Instead, Plaintiffs cite only to Dr. Bernd Klosterhalfen's report from the TVM study. Resp. at 19. Dr. Klosterhalfen's report noted: "Infection is commonly observed following erosion in the vaginal mucosa. Primary infection without mucosal erosion is seldom found." Wave 1 Resp. Ex. R.

Even if Dr. Klosterhalfen's non-peer-reviewed observations from a single report were the type of material pathologists normally rely on in forming their opinions, this report does not support Dr. Iakovlev's infection opinions. At most, the report shows a potential correlation between infection and erosion; but it is axiomatic that correlation is distinct from causation. Dr. Iakovlev cannot reliably extend Dr. Klosterhalfen's observation of a "commonly observed" association between infection and erosion to a categorical rule that erosion equals infection.

Further, Dr. Klosterhalfen's observation only suggests that an infected mesh will likely be eroded. Conversely, Dr. Iakovlev seeks to inform the jury that the presence of erosion conclusively proves infection. *See* Mot. Ex. X, Iakovlev 3/13/16 (*McBrayer*) Dep. Tr. 14:2–6; Mot. Ex. Y, Iakovlev 3/4/16 (*Funderburke*) Dep. Tr. 25:12 (same). In other words, Dr. Iakovlev's opinion is that because a patient's mesh has eroded, the patient had a wound infection by definition. This is a logical fallacy,⁶ not a reliable basis for Dr. Iakovlev's infection opinions.

IV. Dr. Iakovlev's Failure To Follow The Methodology Used By Pathologists To Orient Specimens *In Vivo* Renders His Opinions Regarding Mesh Folding And Deformation Speculative And Unreliable.

In its Motion, Ethicon explained that Dr. Iakovlev's opinions regarding mesh folding, curling, and deformation are unreliable because he failed to follow the standard methodology used by pathologists to determine how the mesh was oriented *in vivo*. Mem. at 18-19. In Wave 1, this Court excluded Dr. Iakovlev's mesh folding and deformation opinions "to the extent they rely solely on his personal analysis of pathology slides[.]" Wave 1 *Daubert* Order, at 8.

Again, Plaintiffs failed to account for this Court's Wave 1 *Daubert* Order, and instead simply re-assert their arguments from their Wave 1 responsive briefing. *See* Resp. at 18-19. Plaintiffs failed to identify any basis for this Court to reconsider its Wave 1 *Daubert* Order, and the Court should reject Plaintiffs' arguments on this basis alone.⁷

In addition, Plaintiffs improperly claim that Ethicon "misrepresents the record to the Court" when it asserts that Dr. Iakovlev's mesh deformation opinions are unsupported and

⁶ Specifically, "[t]his is the fallacy of affirming the consequent introduced in the elementary study of logic, often in the form: 1) if there were an invisible cat in the room I couldn't see it; 2) I can't see any cats; 3) therefore there is an invisible cat in the room." *Toussant v. Good*, No. 3:05-cv-443, 2008 WL 2994768, at *2 n.1 (W.D. Pa. 2008).

⁷ In their Wave 3 response, Plaintiffs asked the Court to reconsider its Wave 1 ruling with respect to Dr. Iakovlev's mesh folding and deformation opinions. Plaintiffs' response to Defendants Ethicon's Motion to Exclude the Opinions and Testimony of Vladimir Iakovlev [Doc. 2959]. As discussed in Ethicon's Wave 3 reply, all of Plaintiffs' arguments were baseless. Defendants' Reply in support of Motion to Exclude the opinions and testimony of Vladimir Iakovlev [Doc. 3054]. In any event, Plaintiffs appear to have abandoned that request in the context of Wave 4.

“novel.” *See* Resp. at 18-19. Plaintiffs conflate two related, but distinct arguments made by Ethicon. As the Motion makes clear, Ethicon first explained that Dr. Iakovlev’s “compartment” theory was “novel” and lacking in support from the scientific and medical literature. *See* Mem. at 18. This is because Dr. Iakovlev’s Report does not cite any scientific literature to support his theory that interactions between mesh and scar tissue forms compartments *in vivo*. *See* Mot. Ex. D, Iakovlev Report at 11-12, 14–19.

Turning to Dr. Iakovlev’s opinions on mesh curling and deformation, Ethicon explained that Dr. Iakovlev failed to follow the well-established methodology used by pathologists for determining how a specimen appeared *in vivo*. Mem. at 18-19. Ethicon also showed that Dr. Iakovlev admitted that he cannot determine whether any alleged deformation he observes occurred during the implant surgery. *Id.* at 19. Finally, Ethicon demonstrated that Dr. Iakovlev did not properly consider the effects of the specialized tissue in the pelvic floor on the mesh during and after the explant surgery. *Id.* at 19 & n. 12.

Plaintiffs did not respond to any of Ethicon’s arguments. *See* Resp. at 18-19. Rather, they again seek to re-cast Ethicon’s methodological challenge, claiming that it is a mere difference of opinion among the parties’ experts. *See id.* But Plaintiffs’ responses simply do not apply to the arguments advanced in Ethicon’s Motion and fail to account for this Court’s ruling in its Wave 1 *Daubert* Order. For these reasons, as well as those discussed in Ethicon’s Motion, the Court should exclude Dr. Iakovlev’s opinions regarding mesh folding, curling, and deformation.

V. Dr. Iakovlev’s Opinions Based On His Mesh Samples Are Unreliable.

In its Motion, Ethicon explained that Dr. Iakovlev should not be permitted to offer opinions based on pathology slides of mesh explants not at issue in this litigation, many of which were from unknown origins. *See* Mem. at 20. In its Wave 1 *Daubert* Order, the Court precluded

Dr. Iakovlev from offering opinions based on such slides on the grounds that his opinions were unreliable. Wave 1 *Daubert* Order, at 11-12.

Again, Plaintiffs failed to account for this Court's Wave 1 *Daubert* Order, and instead simply re-assert their arguments from their Wave 1 responsive briefing. *See* Resp. at 19-20. Plaintiffs failed to identify any basis for this Court to reconsider its Wave 1 *Daubert* Order, and the Court should reject Plaintiffs' arguments on this basis alone.

Furthermore, Plaintiffs' arguments are baseless. For example, Plaintiffs assert that Dr. Iakovlev's meshes came from Plaintiffs in this case, peer-reviewed literature, or Dr. Iakovlev's own prior reports. *See* Resp. at 19-20. Even setting aside the Court's Wave 1 *Daubert* Order, Plaintiffs' position ignores the Court's numerous rulings on this precise issue. *See, e.g., Carroll v. Bos. Sci. Corp.*, No. 2:13-cv-11601, at 23–24 (S.D. W. Va. May 6, 2016) [ECF 105] (excluding Dr. Iakovlev's general causation opinions based on his mesh pool); *Bethune v. Bos. Sci. Corp.*, No. 2:13-cv-06199, at 23–24 (S.D. W. Va. May 6, 2016) [ECF 93] (same).

Plaintiffs do not dispute Dr. Iakovlev's admission that many of those meshes came from plaintiffs' counsel in mesh litigation. *See* Mem. at 20. Nor do they address the fact that Dr. Iakovlev testified that he could not determine the origins of many of his slides. *See id.* at 20.

For the reasons identified in the Court's Wave 1 *Daubert* Order, the Court should exclude Dr. Iakovlev's opinions based on meshes not at issue in this litigation.

VI. Conclusion

For the reasons identified above and in Ethicon's Motion, Ethicon respectfully requests that the Court grant its Motion to Exclude the Opinions and Testimony of Dr. Vladimir Iakovlev.

Respectfully submitted,

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**IN THE UNITED STATES DISTRICT COURT
FOR THE SOUTHERN DISTRICT OF WEST VIRGINIA
AT CHARLESTON**

IN RE ETHICON, INC., PELVIC REPAIR SYSTEM PRODUCTS LIABILITY LITIGATION	Master File No. 2:12-MD-02327 MDL 2327 JOSEPH R. GOODWIN U.S. DISTRICT JUDGE
THIS DOCUMENT RELATES TO: WAVE 4 CASES LISTED IN MOTION EXHIBIT A	

CERTIFICATE OF SERVICE

I hereby certify that on May 4, 2017, I electronically filed the foregoing document with the Clerk of the Court using the CM/ECF system which will send notification of such filing to CM/ECF participants registered to receive service in this MDL.

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